

0050.1491-005 Docket No.:

Title: Genes Determining Cellular Sententing C cence...

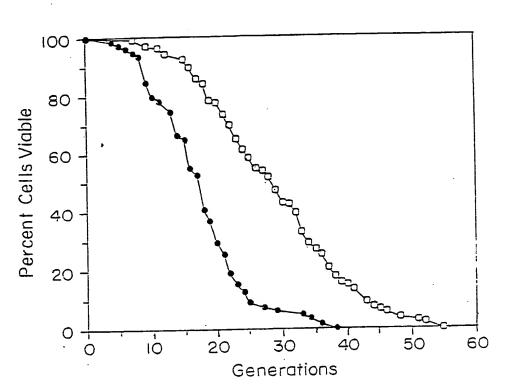


FIG. 1

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Sen ce...
Inventors: Leonard P. Guarente, et al.

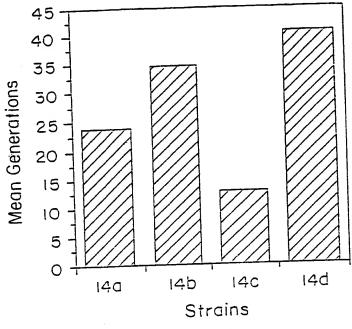


FIG. 2A

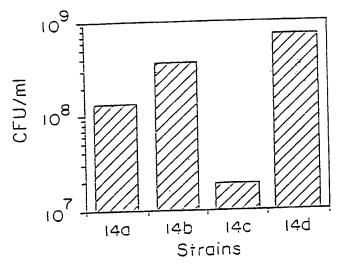
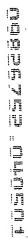


FIG. 2B

Title: Genes Determining Cellular Sene inventors: Leonard P. Guarente, e



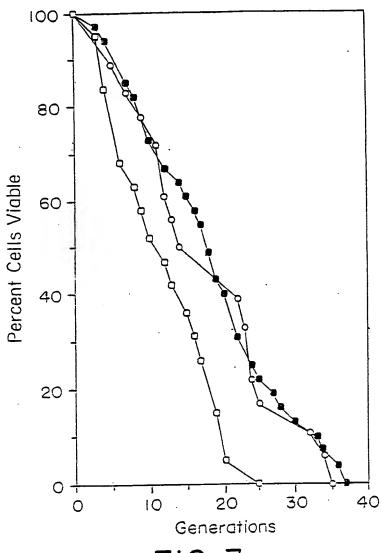


FIG. 3

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Ser

Inventors: Leonard P. Guarente,

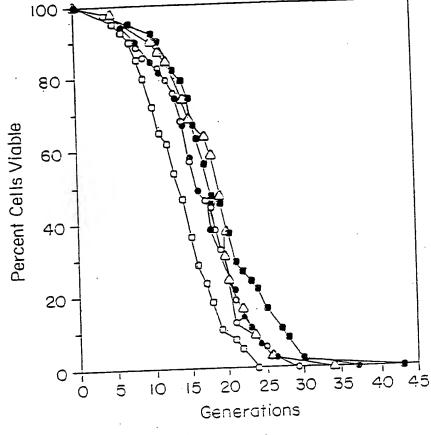


FIG. 4

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Sene Conce

Inventors: Leonard P. Guarente,

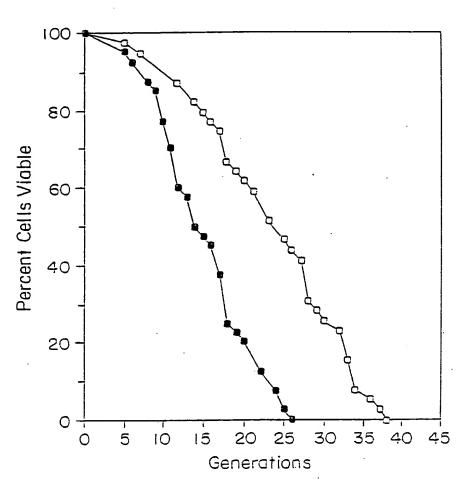


FIG. 5

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Sergence. Inventors: Leonard P. Guarente, al.

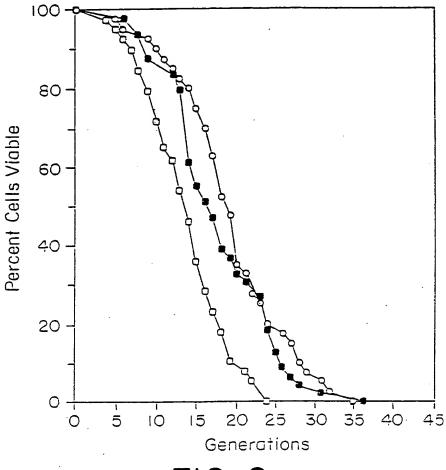


FIG. 6

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Ser

Leonard P. Guarente Inventors:

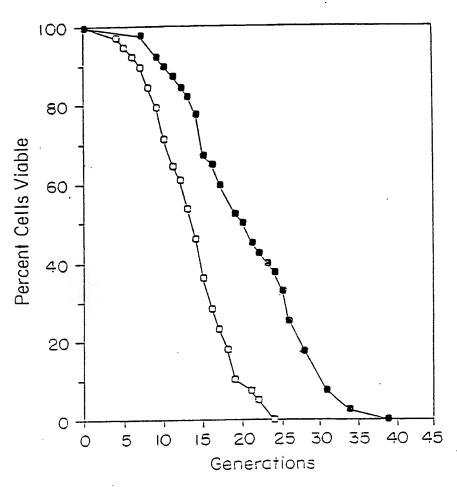


FIG. 7

Title: Genes Determining Cellular Senescence...
ventors: Leonard P. Guarente, el

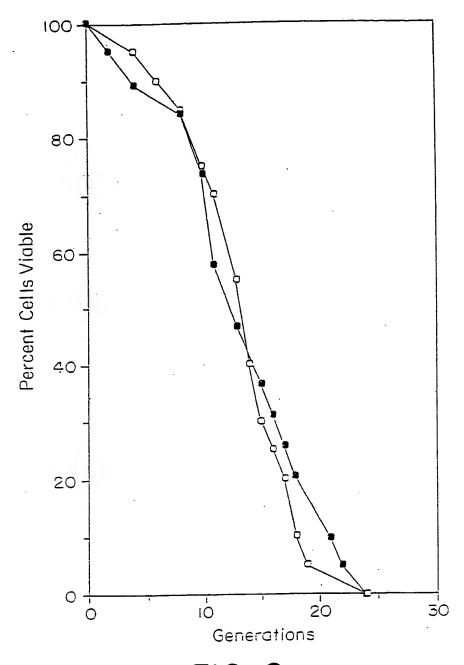


FIG. 8

0050.1491-005 Docket No.:

Title: Genes Determining Cellular So Inventors: Leonard P. Guarent cence...

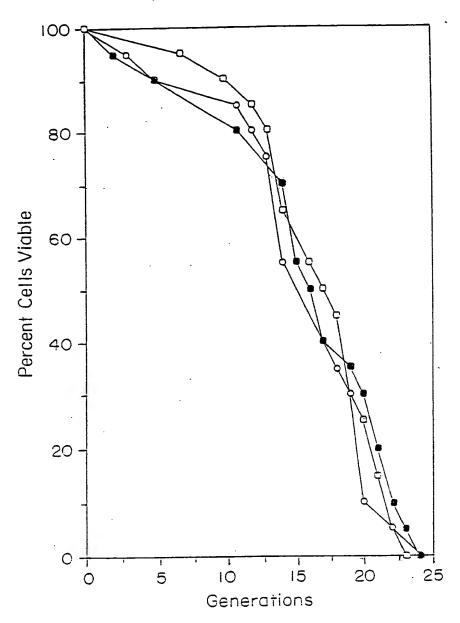


FIG. 9

Title: Genes Determining Cellular Senescence... Leonard P. Guarente, e ventors: 100 80 Percent Cells Viable 60 40 20 0 10 50 40 20 30 0

FIG. 10

Generations

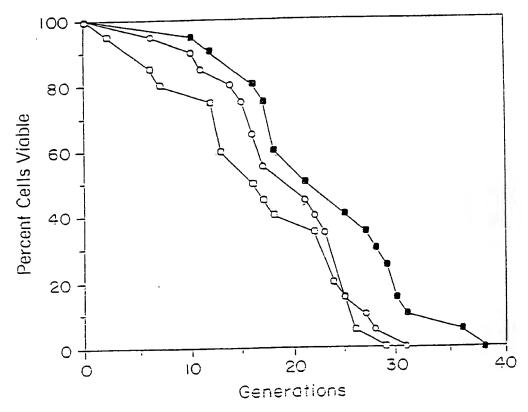


FIG. II

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarent al.

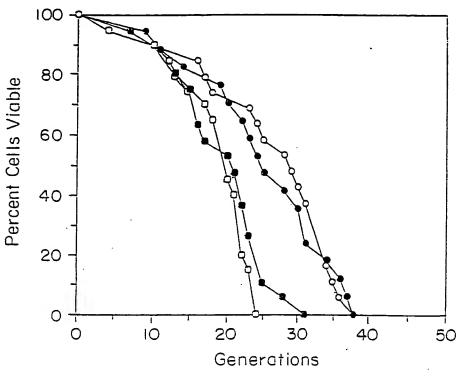


FIG. 12

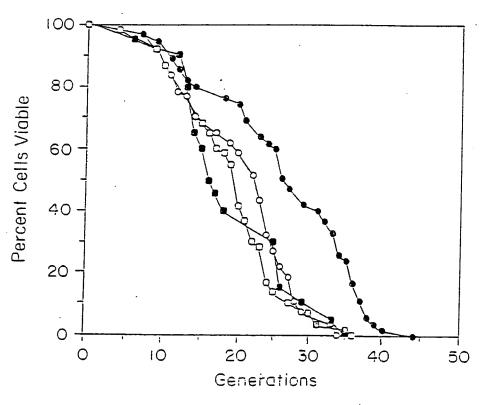
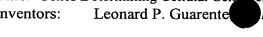


FIG. 13

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarente



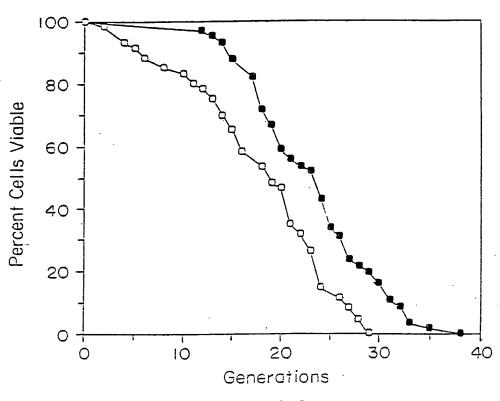


FIG. 14

Title: Genes Determining Cellular Senescence...

nventors: Leonard P. Guarente,

96	188 2	288	369 16	444	51.9 66	594 91	669 116	744	819 166	894 191	969 216	1044
'I'GAAAAAGII'GGAACTAGACCCACGTI'CAGCGGGCCTAGGCCTTCA ATG TGT TAG AATACACAGCGTGCCTAGTTCCTGGTGCCTGGATCTCGAGG 96 3	CCGCGGCACTGGAAAAGCCCTTTTCTAGATCGGGAAACCTA ATG AGT CCA TAA AAAGAA ATG TAG AGGTGGTGTTGACGTTTTGCCGC 188 A S P * A M T * A M T S B S B T T M T S B T T M T S B T T M T T M T T M T T M T T M T T M T T M T T T M T T T M T T T M T T M T T M T T M T T M T T M T M T T M T T M T T M T	TTTTGGCCAAGTAGGTCTTTTTTGCACGGCCCGGGCTCGTGCGGAAAAAAAA	TCCTGATTCGGGTATATAAGTGAATACCATCTA ATG TGT TTC CTT CTC GAG ACC TCG GCG TCT CCC AGA TCA AAG CTC AGC 369 M C F L L K T S A S P R S K L S 16	AAA GAT TTT AAA CCG CAA TTT ACG CTC CTT TCA TCG GTA ACT AAG AAA AAA AAA AAA GTA CGA CCA CAC AAT 444 K D F K P Q F T L L S S V T K K K K K V R P H N 41	TTC CAG TGT ATT CAT TCC TTA AAC TTC GTT TAT TTT TTA TTC ATT CAT TTA TTA TTT GAA TAT AAC CAA CTA 519 P Q C I H S L N P V Y P L F I H S F L F K Y N Q·L 66	CTA GTC CTT CCT TTA AAC AAA AAT TTA AAA TTT TCA AGA AAT TCC AGT ATG AAA TTA TCC GCT CTA 594 L V L P L N K N L P S L N F S R N S S M K L S A L 91	TTA GCT TTA TCA GCC TCC ACC GCC GTC TTG GCC GCT CCA GCT GTC CAC CAT AGT GAC AAC CAC CAC CAC AAC GAC 669	AAG GGT GCC GTT GCC GTT ACT CAG TAC GTC AAC GCA GGT GTT GTT ATT CCA GCT GCC ACC ACC GCT 744 K R A V V T V T Q Y V N A D G A V V I P A T T A 141	ACC TCG GCG GCT GCT GAT GGA AAG GTC GAG TCT GCT GCT GCC ACC ACT TTG TCC TCG ACT GCC GCC GCC 819 T S A A A D G K V K S V A A A T T T L S S T A A A 166	GCT ACT ACC TCT GCC GCC TCT TCT TCC TCT TCC TCT TCC TCT TCT	GGA GAT TTT GAA GAT GGT ACC ATT TCC TGT TTC CCA TCC GGA CAA GGT GCT GTC TCC TTG GAC TGG TTA 969	GGT CTA GGC GGC TGG GCT TCC ATC ATG GAC ATG AAC GGT AAC ACC GCC ACC TCT TGT CAA GAC GGA TAC TAC TGT 1044
FF	97	189	289 J	370 1.7	445	520 67	595 92	670 117	745 142	820 167	895 192	970 217

Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarente,

1119	11.94 291	1269 316	1344 341	1419 366	1494 391	1569 416	1644 441	1.734 451	1.809 24	1894 1	1946 17
					C)		<u>.</u>	A.T.	<u> </u>		
. GGT G	200 9	ATG M	TGG W	GGT G	: TTG	ACC T	, ACT	TTC	TAT Y	VTG	
GTT V	CAA	AAC N	CAA	TGG W	TAC Y	TCT	GTT V	TCCC	FTT	AA 1	
TCC S	GGT G	GAA K	TAT Y	ATC I	ACT T	ე ეეეე	TCA S	I'TAC	CCC	AAAA	
AGA R	GAA K	TCT S	T'AC Y	TGT C	ATC I	GAT D	GTT V	rttr	TAT Y	AAGA	
ggt g	GTA V	GGT G	TCC S	ggt G	GGT G	ACC T	ACT T	PACT	TAC Y	\GTC	
GAT D	TGT C	CCA P	GAC D	GAT D	GAT' D	GCC A	TGT' C	TAG	$\mathop{\mathrm{TTG}}_{\mathbf{L}}$	AAAA	
TCC S	TTG L	TAT Y	GAG K	GAA K	ACT' T'	GTT V	GGT G	GCCTTTTTTTCCTTGAATATTGCAAATAAGCTTTTTGCTAGTACTTTTTTTT	CAC AAT ACA AAA AAA CAC AGT CCT TTG TAC TAT CCC TTT II N T K K II S P L Y Y P F	ATATTATCATATATGCATATTATATAACATAAAAAGTCAAGAAAAAA ATG M	
CCT P	AGT S	GAT D	AAG K	GTG V	T'AC Y	ATC I	GAC D	AGCT	AGT S	ratai	<b>6</b> 1
CAA	AAC N	ACC T	ATC I	TCT S	GGT G	AAG K	TCT S	ATA.	CAC II	\T'TA]	TTG(
GAA CAA CCT K Q P	ACT T	GGT' G	GTC V	GTC V	GC'F A	ATC I	299 299	rgcau	AAA K	3CAT/	TGA *
TCT S	GAC D	TGT C	AAC N	GGT G	GGT G	AAC N	TCT S	rtat'i	AAA K	PATAC	GAA TGA TTGC E *
CCT P	ACC T	ATC I	ATC I	GCT' A	TTG I,	T'TT F	g G	rtga <i>i</i>	ACA T	CATAI	$ ext{TTC}$
rgg W	AAC N	GCT A	CCA P	AAC	GTC V	AAC	TCT S	rrcci	AAT N	rtatc	CAT TTC (
CAA	TCC S	ATT T	CAA Q	NAC N	GTT V	CCA P	TAC Y		CAC II		TTG L
ACC T	cgT R	TCC S	rcc S	GTT V	CCA P	GCA A	GTC V	GCC	1"IC F	TAG *	TTT F
AAG	T'AC Y	ეეე ეეე	TCC S	T'AC Y	GCC A	GAA K	GGT G	TAG *	T'T'T F	CAC H	CT'r L
GCT	TTA L	TCC S	GGT G	TAC Y	T'GG ₩	AAA K	AAT N	TAC TAG Y *	TCG S	T'AC Y	TAT Y
TAC Y	AAA K	GTC V	GCT A	CAA Q	AAC N	AAC	GAA K		AGT S		
GG'T G	GGT G	AAG K	300 0	GCC	GGT G	NAC			ATT I	T'TA L	ACT T
						CCA P			TCA S	.h.dd.	ATA I
	AAG K		GTA V	ACC T	GGT G	AAC		AAC	T'T'T' F	1 <sup>1</sup> Ը"Ր Տ	TCT S
TGT C	TGT C	GCT A	ACC T	AAG K	TCC S	CCA P	GC'T A	GC'I A	T'A'T Y	T'I'I' F	CTT L
	TAC Y	CAA	CCT P		GGT G		GGT G	TCT S	GTT V	ATTT I	TCA S
TAC Y	'I'T'A L	GCT A	G'l'T V	GGT G	GAG K	ATC J	AAT N	GGT G	ATG M	ATTT I	TTA 1.
TCT S	GG'T G	TCT S	G1'C V	A C	ACT T	rcc s	GTC V	TCT S	4.4.	TTC	ምም የ
1045 242	1120	1195 292	1270 317	1345 342	1420 367	1,495 392	1570	1645 442	1735 1	1810	1895 2

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guare



Docket No.: 0050.1491-005

Title: Genes Determining Cellular Se

Inventors:

Leonard P. Guarente

cence...

GAAA

E

K

S

S

ACT

L

C

C

C

C

C

T

T

T

T

T

T

ACT

F

L

L

L

L

S

AACT

F

R

AACT

R

R

AACA

R

R

R

R

R

R

R 

781/261 CGC TTG R L D 841/281 TGA ATA \* I E \* I C L D 801/301 GCA ACT A T C Q L D N S 961/321 ATG AGT M S \* V E F 1021/341 TTG CTC (1 L L D C S A C S A \* V E F 1021/341 TTG CTC (2 C S A

FIG. 16C

Title: Genes Determining Cellular Senescence...

Inventors: Leonard P. Guarent

Invent

1/411

TCA AAC 1
S N 1
S N 1
O T
K L
1/431
GTG AAT C
V N E
S N E
I L
TTA TTT T
L F W
Y F
I L
AGC AAA A
S K R
A
AGC AAA A
S K
A
I V R
C
I V R
C
I V R
C
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I
I S I 11231 Y Y Y 1291 1291 1291 1291 1411 14 

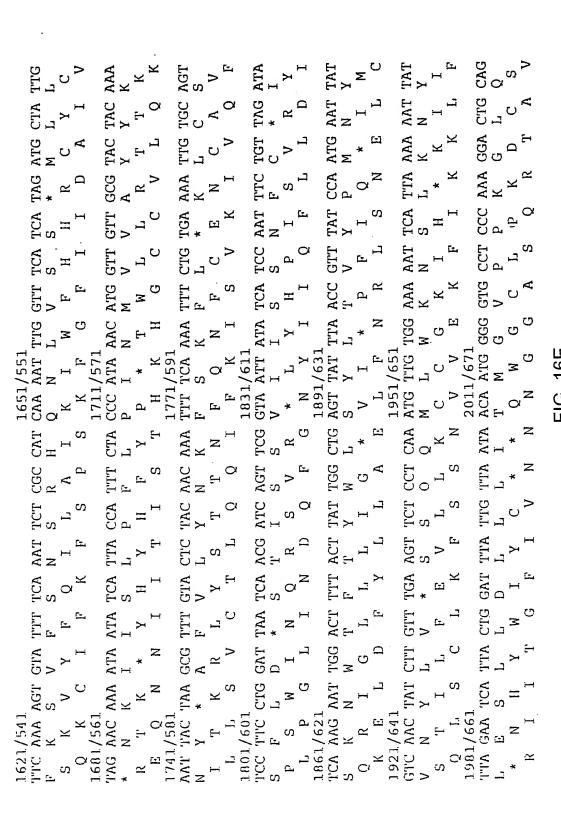
FIG. 16D

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guaren



Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

GGC AAA ACA GCT CTA GTA CAT TGA ATT ACG GTA ACT TTT GTA ACG ATT TTT CAT TGA AAA

2251/751

2221/741

2281/761

2341/781

TAT TAG ACG TITA AGA ATT ATT CITC CITC TGC TITG CTT ACA ACA AAA ATA GTA ACG CAA TITG

4

2191/731

THA ATG TGC TAA TCA GGG ATA ATT TTG GTA ATT

ICA CAG TICA AITT

o Z

Ö

I'NG CI'T CIG AIG ACG TGA I'NA AIG CIT CIA

Inventors:

Leonard P. Guarent

ATA ACA ATC TIC AAA CGA TIA ACA ACG AAA CAA AGA AAA ITA AGT IGA AAG TIA AAG CTT ATG CAG AAG CCA CAG GTA TAC CAT TCA CTG THE GTA ACT TEA THE TEE THA CAA AAG AAT TAE THE CAA GTA TTA AAA CTA CAT CET ATG 2311/771 2431/811 ACA TAT CTC CTC AAG TCA CTG CAA TGA GTC T R

0050.1491-005

Docket No.: 0050.1491-005
Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarente,

	ATG.	₹.	ပ	K		CAG	a	ß	K		ATG	æ	ບ	Ø		ATC	Н	ಬ	႖		ACT	H	1	ß		C <u>I</u> C	ч	ಲ	4		99	ا ق	ල ්	IJ
	VCC 7	-	д	=		IAC	` >-	H	д		AAT	z	н	×		CAT	=	H	×		ATA	н	*	Z		CIG	,,	ပ	K		CAA	ď	× '	<b>~</b>
	ATA 1	н	*	Z		CILL	ı	Į <b>E</b>	IJ		NCC	H	Ъ	ø		ACG	H	<b>~</b>	4		ည္ပ	A	д	=		ATT	H	îz.	ß		TLL	5±4	ĬZ.	ß
	MIC	н	ໝ	×		TIL	ĵ.	<u>54</u>	Ø		CAA	ø	×	z		AAA	×	×	Z		TAA	*	×	Ŋ		CTA	Ţ	*	Z		ATG	X	ນ	>
	NI'A AGA ACC CCC ATA ACA AAA ATA GIC ATA ATC ATA ATC ATA ATC ATA ACC ATG	<b>,</b>	*	H		ATT	H	Ē	A T I S II R II I S I D A A II I S L P A		TCT	တ	н	ß		CAC AAG ATC AGA AAA TTC ACT CTC CGC AAC AAA TTA TGA ACT TCA ACC AAA ACG CAT ATC	L	д	ø		1766	PRWEHLLSILKLTHHW*AIT	ဗ	>		ATC	H	V T K L R Q P P V C K F N G T S * F C C	Д		CTA	H Q S I R S H H L T L P M * I L M F Q G	*	Z
	ATIC	H	ß	Ħ	2551/851	O.I.C	>	ß	=		ATT	H	Æ	îz,		TCA	သ	ø	z		CAT	=	H	1		CAC	=	T	=		ATC	j.	တ	Д
	ATA	H	*	z		သူ	д	а	×		ATA	I	*	Z		ACT	Ţ	ч	14		CAC	н	터	д		7GG	3	Ö	A		1GA	*	田	z
	ATC	H	ಭ	Ħ		ATA	H	×	H		CCA	Ь	Ø	Z		TGA	*	Ħ	Z	_	MCC	Ħ	Д	Д	_	TAA	*	Z	Σ	_	MTG	Z	ບ	>
2491/831	ATA	H	*	z	/851	GIC	>	ಬ	Ξ	7871	TAA	*	z	H	1/891	T'TA	1	×	Ξ	1/91	CTA	ı	*	Z	1/93	ATT	H	Œ	Ţ	1/95	CCA	Ъ	œ	z
2491	ATC	H	တ	=	2551	AGA	œ	된	ໝ	2611	CTG	J	ບ	>	267]	AAA	×	z	H	273	MAA	×	z	Ħ	279	CAA	ŏ	×	Z	285	TTA	Ľ	X	₽
	ATA	H	*	Z		AAA	×	×	×		GCT	K	J	ß		AAC	z	H	œ		CIC	Г	ß	œ		TTG	П	ບ	A		ACA	T	=	H
	G'IC	>	ಬ	Ξ		ATC		ູໝ	a		ACA	H	0	ន		ည္သ	<b>~</b>	4	ø		ATT	н	ħ	ß		AGT	ß	>	ĬΞ		CTA	1	*	z
	ATA	H	*	ß		ATA	H	*	Z		GTA	>	*	Z		CIC	7	ຜ	д		TICA	ß	Ø	Z		ည	K	д	a	1	CAT	Ħ	H	ß
	AAA	×	×	N E N S II N II		ATA	н	*	Z		GAA	逆	×	ß		ACT	H	IJ	ß		$CI^{T}$	ı	<b>52.</b> 1	Ħ		ACC	T	Д	~		CAT	=	Ι	Ø
•	ACA		0	<b>'</b>		ACA	I	0	Z		GAA	E	×	×	;	TTC	įz.,	S	=		CTT	ו	ĵz.	ß		ACA	₽	O	Z		TCT	S	7	တ
	ATA	H	*	Z		ATA	H	*	Z		ATA	н	*	×		AAA	×	z	H		CAC	=	H	Ъ		TCG	ល	×	0		CGT	¥	>	Ħ
	ညည	ď	д	H d l		A'I'A	_	*	Z	•	ACC	=	Д	=	)	AGA	<b>~</b>	ㅂ	×		GAG	ы	ល	K		ACT	H	1	يحز		ATT	Н	Ē	മ
	ACC	:	Д	<u> </u>		ATA	<b>;</b>	*	z		CTT	1	ı	<b>×</b>	١	ATC	H	တ	O		16G	3	Ö	Ö	_	AAA	×	×	Z	_	1CC	ន	Д	=
1461/821	AGA	~	ы	z	2521/841	ACA	<b>E</b> -	, 0	z	/861	A'I'G	Σ	ບ	<b>4</b>	1/88	AAG	×	~	Ω	[06/1	CGA	~	Q	Σ	1/92	TAC	7	1	0	1/94	CAA	a	z	H
2461	A'ľA	H	*	×	2521	CIC	T	ß	=	2581	CTA	1	*	Z	264	CAC	=	H	0	270.	CCT	24	-	ß	276	CGT	~	>	Ï	282	CAC	=	ī	Ч

GAT TITA AGC AGC CTG GAT TTA TGA TGA ATG AAA CCG ACA AAA TTA ATG CTA ATC ACT TCT

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Leonard P. Guare

Inventors:

AAT GIC AAG GCC CAT ATA ATC AAG TTA ATA TGA GCC GCA ACG CTA GTA TTT CCA ATA TGC CTG CCA THE TIT THE TITE CET THE THE THE ACA ANT ATT THA CGE AGA ANT CAN AGA CAN ANG ANA TGA ATA CCG CTA GAA CAT CTG ATG AAC TTC AAT TCA CTT TGC CAT AAT ACT TTT TTT TCT AAT AAA AAA TAA AAA ATA AAA AAT TCA ACT AAG CAA TGA CGT CCT ACT AAA GTC CCA AAA ATC AAA CGG AAG GTG CAA ACT GGG ATT CAA GTT TGT CAA TGA AGT CGC AGC CGC CAT ACT CTA ATG CAA ATA GTC AAA ACT TCA ATG AAT CTT TTG TGC 3091/1031 3151/1051 3211/1071 3271/1091 3031/1011 2971/991 ល U 3001/1001 3061/1021 3121/1041 3181/1061 3241/1081 2941/981

ß

3331/1111

3301/1101

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Inventors: Leonard P. Guarer

THE GAA CAE GITA THE ANA ATHE CITE CEA CITE CET TITE CAG GGT TAG CAT THE THE THE CITA CEA I'I'T GAG CCG GAA AAA AAI' GGI' AAA GCA AAC I'AT I'GC CAI' C'I'I I'AT AIT 1TG I'AI' I'CT GTIT AAA TGA TCT AAT TTT TTG AAT CGT TTT K \* S N F F L N R F 3421/1141

FIG. 16

TAT CIG ICC AAT ACC GIT GCC TIN

1/1 GTG TCT TCC ATG GAG TGA ATT GTG ATT TGT GAA TTA

181/61

241/81

Title: Genes Determining Cellular Senescence... et al.

Inventors:

Leonard P. Guar

GITT ATC TCT CIC CGA AGG TGA ACA GCA AAC TIG TIG AAA CAG AMA AAA AAC TTT TTT TAT TCT THA TGA TCA ATA TAG TAG ATA GTA TAG TTA CTT TTT TTT GAA TAG TTT 301/101 ATC ACT CAG ACT CAA AGA GAA TAT CGG CTT GAC GAT TGT

CIT CCG TAT ATT ACA TTG TAC ATT ATT TTT ATT GTA TTT TAG TTT CCA ACG TTA GGA TTT

0050.1491-005

Title: Genes Determining Cellular Senescence... Leonard P. Guarente Inventors:

CAG Q CIT TAG GIT CIT TITA AGA GIYC IVT GIT CAT TIT CCG ITC TIA CIG ITT CIT IVI CCT CON CGA CIT AAA AIT CCT GIT GAF ATT GIC CAC TAG TIC ICT TIT CAF AIT ITA ITT ICG CIT AIT C'I'N CAA AAG GIT TGA AAG AAG AAA TCG ATG ATG TAG TAG ACC CTG TCG TTT I. Q K V \* K K K S M M Y II Q \* T L S F GCT GTA ACA TTT TTA AGT GGA CCT ACG 571/191 691/231 751/251 631/211 TAT CIT TIA AGA AAG AGA GAA

601/201

541/181

661/221

0050.1491-005 Docket No.:

Title: Genes Determining Cellular Senesence...

Inventors:

Leonard P. Guarente,

TAA ATG ACA ATT CAA TGA AGG TAT TGC CAA TCG CAT GGG CTG ATC CAA TGT TAT TCA. AGA ATG 931/311 CAG AAA CAG TCA ATT CTG CTT TAG AGC AGT TGA ATG THE AGG TITE CITE 961/321

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Se Inventors: Leonard P. Guarente,

																																		•
	CTA	L	¥	H		TCA	ಬ	ø	×		TAA	*	z	H		CTG	1	ပ	>		CCT	а	ľ	ß		AAA	×	z	н		CTA	ľ	¥	Ħ
	၅၁၁	Дı	~	¥		CGT	≃	>	Ŀ		ATG	E	ဎ	T \		CGT	.≃	>	ß		CTC	ľ	ß	Д		TCA	ಬ	a	×		GTC	>	Ø	a
	CCA	а	=	Ħ		GTT	>	<u> </u>	ಬ		ACA	E	ø	Z		AAC	z	Ħ	д		ATA	Ι	<b>&gt;</b>	H		ATT	H	趾	Ēų		AGA	Z Z	田	ß
	AAA	×	Z	Ħ		CT'A	Ţ	*	ಬ		CCA	d,	œ	Z		AGA	æ	Ы	×		ATA	н	*	Z		SSS	ם	~	<b>a</b>		AAG	<u>_</u> ×	~	된
•	AAG	×	<b>~</b>	M		AGG	×	හ	K		550	~	Ö	Z		CTA	ı	*	×		TTG	ī	*	Ω		TAT	×	H	ß		AAA	×	×	×
-	TYIG	ľ	C S II * R N II R Y	缸		ATA	H	*	×		ATG	×	ບ	4		AGG	æ	Ö	4		CIT	ı	Ē	œ		AAT	z	H	ч		CTA	J.	*	×
	CCA	Д.	=	Η		ATA	H	*	Z		TCA	ಬ	œ	Z		CTA	ı,	*	×		TAT	×	H	מ		AGA	~	Ħ	×		CAG	ø	ß	A
	TAG	*	Ø	K	_	CTA	ı	*	Z		TTA	7	<b>&gt;</b>	H	_	TTT	Ē	Ē	ß	,4	CCA	d.	=	H	_	CIG	Ľ	*	Ħ	_	CAC	=	H	<u>ρ</u> .
1231/411	CIG	ı	ບ	>	1291/431	AGT	ß	>	ಬ	1351/451	ACC	E	Ω,	7	1/47	ATT	H	ĵ:	Ē.,	1/49	AAT	z	H	ß	1/51	TTT	î.	ĵz,	ß	1/53	CTG	Г	ບ	K
123	CAT	Ħ	н	Ω	129	999	Ü	Ö	团	135	CIG	ı	*	Ω	141	AGA	<b>~</b>	ы	Z	147	CIC	ı	ß	O.	153	GTG	>	ບ	>	159	AAA	×	z	Ŧ
	CAG	œ	ಬ	Ø		GCA	K	ø	×		CAA	ø	z	Ħ		IGC	ບ	K	a	l	GAA	Ħ	z	H		ATA	H	*	ß		ATA	Ι	*	×
	GAT	۵	Ħ	Ω.		AGG	×	U	Ö		CAC	=	Ħ	Ω,		ACA	=	=	Σ		CCA	ď	a	H		CCA	凸	ø	Z		TTA	ľ	*	z
	CAG	o	~	Ü		CTA	Ţ	* .	×		TAT	×	H	വ		CTG	1	*	Ω		ANA	×	z	E		CAA	a	z	H		TGA	*	Ω	H
	TAC	7	÷	д		CAT	=	H	ß		CIT	Г	<u></u>	ı		AAT	z	H	ß		CAA	ŏ	×	×		၁၃၃	d.	а	ď		ATT	H	Ή	1
	ACG	<b>:</b>	×	>		TAC	¥	<del>.</del>	Д		ATG	Ξ	ບ	K		TCC	Ω	ď	O1		cTG	1	ບ	¥		TAC	×	H	д		NGG	<b>~</b>	೮	Ω
	CAA	ď	×	Z		ည	A	Ц	1		TTC	ĵz,	ß	Ξ		ACT	1	1	<u> </u>		ATA	H	>	₽		TTA	ľ	×	H		AGG	æ	ບ	떠
	ATT	<b>-</b>	Ē	ß	•	AAA	×	×	ß		CTT	'n	<b>54</b>	노		MGG	<b>×</b>	O	Ω		ACA	T	a	Z		CAT	=	H	<u> </u>		CGA	<b>*</b>	티	×
_	CIC	1	ß	=	_	AAG	×	~	円	_	AAA	×	z	Ŧ	_	CAA	Œ	×	×	_	CTA		*	Z	_	CGT	æ	>	ß	_	CCT	д	1	ß
1201/401	TAT GGA CTC ATT CAA ACG TAC CAG GAT CAG CAT CTG TAG CCA TTG AAG AAA CCA CCG CTA	G L I Q T Y Q D Q H	Ω	<b>-</b>	1261/421	TAC	¥	STRKPTI*GQGV***G*FVQ	ø	1321/441	GAA GAC AAA CTT TTC ATG CTT TAT CAC CAA CTG ACC TTA TCA ATG CGG CCA ACA ATG TAA	2	H	ROTFIRALSPTDLINA	1/46	TGT	၁	>	Ω	1441/481	GAG	* K L T I L Q K P E L N P Y L L I I L P	တ	¥	1/50	CCII CAA CGT CAT TITA TAC CCC CAA CCA ATA GTG TITI CIG AGA AAT TAT CCG ATT TCA AAA	ď	z	H	1/52	AAA	×	z	ETSKEDLINKTAPAKKESPT
120	TAT	<b>×</b>	Ξ	3	126	C.IC	1	ಬ	-	132	GAA	E	×	<b>~</b>	138	CCI	_ 	1	1	144	TAG	*	<b>~</b>	U	150	CC.I.	Ь	1	ຜ	156	TAG	•	~	e)

1651/551

1621/541

0050.1491-005 Docket No.:

Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarente

	J.C.C	ບ	, <b>«</b>	a		ATT	H	Ē.		ì	ATT	H	ь	ß	1	TTT	ĵz,	œ	1	ł	CCA	ď	=	Ŧ		TTG	I,		ဗ		CCT	FP.	1	3	
	TTA	Ţ	<b>&gt;</b>	Σ		CTA ATT	Ţ	*	Z	:	GIK	>	ಭ	=	:	CAG TTT	ŝ.	ໝ	>		AGC CCA		æ	a		ATC	H	വ	1		CIC	Ţ	ß	д	
	CTA	,	<b>&gt;</b>	H		TTC		70	ď	ı	CGA	2	<b>E</b>	Ø	1	CAC	=	H	д	ı	GTA			¥		CTA	L	*	Z		CIC	ľ	ß	đ	
	ATC	Н	ໝ	đ		CTT	ı	Ē.	íz.	,	CTA	7	×	H		TIG	1	ဎ	4		GTG	>	3	೮		ATC	H	ß	đ		ညည		Д	Д	
	CAA	0	, ×	Z	٠	T'TA GAT CAC	Ħ	TF	a	I	TCT CIC CGA T'IT TAA ATC CTA CGA GIC AIT	<b>;</b> (	83	A	)	ATC	H	τΩ	J	i	ATG	Z	3	೮	1951/651	TAA	*	N K S	z		သည	a	Д	Д	
	AAC	z	H	4		GAT	۵	W Y * I	ß		TAA	*	×	Z	i	TTC	Ē4	Ø	=		ATG	Z	*	Q		TAA	*	z	H		ACA	H	=	H	
	TTC	ţz.,	ß	O	!	TTA	Ţ	*	æ		TTT	Œ.	54	17	i	CAA	ø	z	H		AGA	æ	되	Z		ATT	H	ÎΞĄ	1	2011/671	AAA	×	×	N O O d d	
_	TAC	<b>&gt;</b>	H	7	1/571	GTA	>	×	H	-	CGA	2	۵	H	-	ည္သ	~	Æ	4	_	TGA	*	H	×	_	TGG	3	ပ	Ω	_	AGC	ß	4	ø	L
CC /T	CIT	ı	ĵe.	J	1/57	ATG	X	3	Ö	1771/591	CIC	1	ß	Д	1/61	AAT	z	H	ß	1/63	ATA	<del>  </del>	×	Σ	1/65	GGA	ບ	_	Σ	1/67	၁၁၁	Ω,	д	œ	7
COT	GAC	Д	H	ρı	1711/	2	rn	П	•	177	TCT	ß	1	S	183	ည္သ	O.	댸	a	189	CAG	œ	æ	Ω	195	TTA	1	*	~	201	CTC	1	ß	д	C
	8	ဗ	೮	Ö		CTA	ı	P Y	H		AAC CTT	1	T F	124		TAA	*	z	H		TTT	بحا	Ēų	Ω		ATG	E	ບ	>		TAC	×	Ħ	д	
	ATG.	×	×	Ö		ည္သ	4	ď	а		AAC	Z	T	C4		CIC		S			CCT	G	Г	Ē		CAA	æ	S	Z		TAT	×	Ħ	1	
	CAT	=	H	X		CCT	Д	1	຺ໝ		TTC	F	ß	O	ŀ	1.10	<u> </u>	ໝ	4		TIG	ı,	ບ	Ø		GIC	>	Ø	д		ACA	Ħ	=	Ħ	
	AIC	H	ß	д		TAT	×	H	ಬ		ATG AAA TGG GCG CGC AAT TTC	'n Z	H	ţzų		CAA	Ö	<b>z</b>	<b>H</b>		CTA GIT CAA ATT CTG TTG CCT	ı	* F K F C C L F	>		999	۲	೮	O		TCC	ល	Ъ	Ħ	
	CAT	=	H	7		ATA	Ħ	×	H		ည	z z	A	œ		CIC	1	ß	а		ATT	H	Ē	S		AGG	<b>~</b>	g	V		C'I'I'	ľ	ξų	Į.	
	CAG	œ	ß	<		ATA	H	*	z		925	A R	<b>~</b>	K		ATT	H	ß.	ß		CAA	ø	×	z		ACA	Ŧ	ø	×		MAC	z	IJ	വ	
	GIG GIG	>	ပ	<		CYC	=	H	=		17GG	3	G	Ö		CAA	ď	×	z		<b>G'I'T</b>	>	Ē	ß		ACG	H	~	Ω		73	ပ	K	æ	
4	ATG	Σ	3	Ü	_	ACC	H	Сı	24		AAA	×	z	Σ	_	ATG	Z	ပ	K	_	CTA	Ŀ	*	വ	_	ATA	H	*	Z	_	CVA	ď	z	Σ	
		7	NINCSISINGTFTSTKSYAA		1681/561	ည	K	R P P T * Y I L P	=	1741/581	A'I'G	M K	*	<u>F</u>	1801/601	CAC TAA ATG CAA ATT CTC CAA TTC CTC TAA CCC AAT CGC CAA TTC ATC TTG CAC	•	×	z	1/62	TAN ACC C	<u>-</u>	24	Д	1/64	CCA CCG ATA ACG ACA AGG CGG GTC CAA ATG TTA GGA TGG ATT TAA TAA ATC CTA ATC TTG	د	= R	<u>α</u>	1/66	CAT	=	H	PSMQPFHILPPQQNTPPPW	
1 1	CAR	a	z	Ţ	168	CVC	ø	~	G	174	CTT	-	-7	<b>&gt;</b>	180	CAC	=	H	7	186	TAA	•	×	Z	192	CCA	പ	=	=	198	ည	ဗ	<	Ъ	

2071/691

GGC TITT ATA GCA CITC CAC CITC CCIT IVA ACG

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Leonard P. Guarer Inventors:

GCT ACT ATA ATA CAT TGT GTA AAG ACC AAC ATG GTT GTC' GTF TTC TGC TTG CGG ACG CAG TTT CAA TGG TTC CGC CTC ATT TGT GCG CCA ATA ATA AAC ATC igt caa gtc ata atg aca atg aca atg gta ait cta TGA AAA ACA THE AGG AGT CGT CGA 2191/731 2131/71 2311/77 2431/811 GIC GIT CTA ACG TIC GTA AAA IGA AAA AIA ACA GCG CGG AAA AAC AAC GTA AAA ACC ANT ATA TCG GAA GTA TTC ACT ACA ATA ATA ATA ATA ATA 2161/721 2221/741 2281/761 2341/781 2401/801 S ď

Inventors:

Leonard P. Guarente,

AAA AGC AGT 1GG ATA 1TC TCG GCA GTA AGG CGG CGG ACC GAA TTT 1TG AAG AAA CTA AGG AGC CTG AAA ACT ATA GAC ACG TIC AAA AAT GIT TGC AAA GGT GGG CAT TAC AAA AAC TCA TCA CAA AAA 2491/831 2671/891 GAA AGG ATT TAA ATG GTA ATC ATG AAG AGG TTA CCA CAG AAC AAA CAG ATG AAG AAG CAC AGA I'CC AGI' T'I'A T'C'T 2641/881 2701/901 2761/921 2821/941

FIG. 17G

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senes

nventors:

Leonard P. Guarente,

GGT GTT GCG TTT TGC AAC GTT GTC TAG ATC ATG GGA CTA CAG AAC AAT GTG ACA ATC TGT TING ATA AAT TAA CIT TGG ATC CAT TIG GCA ACT ATG 3001/1001

IGC AAT ATA TAA TTA CCA AAG AGG CTG AGA AGA ACA AAT ATG ATT ATA CGC

3091/1031 3061/1021

TYC ACC TYCT TYGA AAC CAA GAG CCA TYCG AAC TYTY CTA TYC ATA AAT TYG GAT CAA ATG TYGA

TGG AAA FIG AAA AAA TCT TGA AGA CAG CTA TIG TTT CGG AGC CAA TGA TTC 3151/1051

ATT ACG TIT TAC ANG GIG GCG AGA CGG GTA TITC AAT CAT TGT TGA ATG ATA GCT ACG GAA

AGA CAG CAT TAG ACA TIT CIC ATA AGC AAA ATG ACT ATC TCT ATA AAA GAC TAT CAG AGA 3241/1081

GAA ATA CAC CTC ATG GTA AAA GAA TCA TCG

3331/1111

ING YGG CGC CIT TAC YGG YGG GCC CCA TAA

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Sepescence...

Inventors:

Leonard P. Guarent

TAA ACG TCG CTC CAC AGG ATA CTG TAG AGG TCC TCA AGA CGC CCT AGA AAA CAG AAT GIYI CTT AIY TAA ATA TAG GAA TITI ICA CITI TAT GGT ATA CIG GTA AAT AGC CIC ATA TAA TAT CTT TIG TAC AAT ACT AAA ATA CAT CAT TTT TCA ANT GAA TAT CCA AAG CAA AAA AAA AGT GTT GAA GAA ATA AGA GAA GGA 3541/1181 3481/1161

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarent

ICA CCG TITA ITTA ACA AAT ITCA TCT AGT GTC CCC AAA ITTA AAA CTA GTT GCA GAA AAA TIIG ITA TTA GAT TGG ACT TGC GAA TTA TITT TGC CCA TITT GTT GGT TGC GCG TAA TCG GGA LITG I'I'T G'IG TITC ATA AAT GGT ACT I'GT ACT GAA G'IG GGT ATT I'GC 1'GC 1'GA GCA TIG ATI'T GG'I ITA CIG ITG ITG ITG ITTA ATA ITG ITA ATA ITG ITT ITA NIC ATA ICA GAC ACG GAT AAT GAC CTA AAT GAA GGC AAI 3841/1281 3901/1301

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Serescence...

Inte: Genes Determining Cellular Second Inventors: Leonard P. Guarent

aac atc agg N I R act T gaa gat cgg ggg gct gaa atc cat ctt cat cct acc gct ccg ccc gtg ttg gtg gaa tga cca gcc ctg tcc cag gat cta tag gag ttg cag gcc gtt ccc agg acg acg cta tgg P A L S Q D L \* E L Q A V P R T · T L W agc agc ttg ggg gag gaa gtg gag S S L G E E E V E cay ggt cyc aag cyc agc cac aac cag ctg caa atc agg ctc ttg cag ctg gga ata aca tto atg. cag tgo ttt ggc agg act ctt tca oto and and cay ota ato don aca tgo otg ttg ttt got ata ata aca aac atc gat ggc cta ctg ggg 391/131 331/111 271/91 211/71 151/51 Cag ບ act act tet tte aga gge age atg gtg T T S F R G S M V gog ttg cat gtg tot tga aga gaa aag a s म 301/101 181/61 വ G

1G. 18A

Title: Genes Determining Cellular Senescence... nventors:

Leonard P. Guarente, e

att cag ttt cco ago caa toa tgg tgo aga gaa gao otg gto aga gtt tco atg tga aca I Q F P S Q S W C R E D L V R V S M \* T yac caa aag gaa tat tcc tgg gtg atc aat ggc gag aca gtg cct ggg gaa cat cag atc D Q K E Y S W V I N G E T V P G E H Q I gtg agg tca att ctg tac tgt ccc cac gat cgg aga gtg ggg gac tag gcg tta gca tgg tgc gtt cca tgg atg aac tga atc atg att ttc aag cac ttg ctc tgg agg gaa gag cga c v p w m n \* I m I F K H L L W R E E R tgg agt atg tgt tga gct cat ccc cgg gcg att cct gtc taa gaa aag gag gat ttg Ö Ö 751/251 691/231 571/191 631/211 **~** ಅ tgg gag age tet tge cag gta aaa agt ಭ Ö O 541/181

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Sen

Inventors: Leonard P. Guarente,

tac ctg tgg act cag cag cag caa ctg tgg gac ttt yec aga act cig cta atg aag tgg atc ttc tgg gtc caa acc aga atg tca aag att tta cag acg ccc aga gty tcc cct tgg acc cca tgg caa ggg atg cag aca gtg atg aaa acg tac cag tgc aga atg gga att cag gca cgc agg tag ccc agc

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarente,

							1231/411	/411								
ଅଷ୍ଟ	<u> </u>	att ctc aac aac agc tgt tcc aaa gac cta	tcc	aaa	gac	cta	atg	cgc	ttg	ctg	tca	agc	agt	tga	cag	g tco age agt tga cag etg
ន		່ວ	ß	×	Ω		Σ	` <b>~</b>	ı,	ı ı	Ø	ູ່ຜ	່ຜ	*	ø	
K		>	Д	×	Ŧ	*	ນ	K	ပ	ບ	Д	Ø	>	۵	Ø	ບ
I	-	Œ.	ø	~	а	Z	4	1	K	>	ø	ø	1	H	4	æ
							1291/431	/431				-				
c aq	ىد	atq	CAC	tqq	caq	ctq	ctc	atc	aga	cdc	aca	tcg	gtt	tag	ata	acg
SS		×	=	` *	Ö	ı T	ľ	I	ູໝ	<b>~</b>	<b>=</b>	ខ	>	*	ľ	<u>م</u>
>		ບ	T	ŋ	ໝ	ບ	83	ಬ	K	Æ	=	ĸ	St.	ß	83	<b>~</b>
Ϋ́	$\rightarrow$	K	1	K	V	~	=	Ø	ρ4	=	H	Ö	,	æ	а	K
							1351	/451								
ctg cgt ttg tcc cca at	Ø	ato	cat	ACA	tca	tca	gog	atg	ata	CCC	cag	gga	cgg	acd	cat	aca
а		н	=	Ŧ	S	ន	<b>4</b>	ı	Ľ.	4	ø	<sub>O</sub>	æ		Д	H
O.		ß	H	=	=	ø	<b>~</b>	ပ	ß	Д	ĸ	Ω	Ö	<u>a</u>	7	=
<u>م</u>	Z	Д	X	Η	H	Ω	K	K	д	а	Ü	H	Ω	Д	<b>&gt;</b>	E
							1411	/471								
g	53	cag	cag	cga	cad	tag	gca	cag	ctg	tgg	toa	cta	acc	agt	att	atg
ב	•	a	ď	<u>ہ</u>	H	*	4	œ	ָ י	3	ಬ	ı	Ħ	ß	H	Σ
Ĭ	<b>E</b> )	အ	ຜ	Q	H	~	വ	ß	ပ	Ö	а	ß	ч	>	ı	Z
<b>«</b>	K	×	K	H	7	Ö	д	K	>	>	а	=	Ø	<b>&gt;</b>	X	Ö
							1471	/491								
ر <del>د</del> ج	gg	gag	tot	acc	ctg	CCA	gtc	ttt	tca	aga	agc	aag	ctg	ccd	atg	ccd
9		되	ಬ	Ţ	7	Б	>	ĵz.	S	သ	သ	×	1	ы	ı	<b>4</b>
	Ö	ល	Ţ	Ъ	ບ	ø	ಬ	드	Д	A	K	ಬ	ບ	×	ပ	~
3	O	>	<b>&gt;</b>	а	4	ß	7	Œ	ø	ø	œ	K	4	K	4	Ø
							1531	/511			•					
8	tt	CAG	cta	atc	aac	aga	CCB	CCC	Cac	agg	ctc	agc	aag	gac	agc	aga
	_	ø	.,	H	z	<b>~</b>	<b>4</b>	ď	=	×	7	ល	×	۵	ಭ	Ω.
	5.	S + S + N	*	ន	Ľ	Q	=	Д	<b>E</b>	ບ	ល	.d	æ	H	K	4
z	ß	4	Z	ø	a	۲	H	а	œ	4		æ	O	œ	œ	œ
							1591	1/531								
g.	gag	gag	CCB	gcc	aac	gta	ctt	tga	CCC	саа	acc	aga	acc	aga	agg	gay gag cca gcc aac gto ctt tga ccc caa acc aga acc ago agg gao
-	H	洒	д	K	z	>	,ı	*	а	ø	F	<b>~</b>	Ŧ	ಬ	×	<u> </u>
	~	ß	ø	ď	E	ß	Ē	۵	а	×	겁	뙤	ф	4	Ü	H
V L R G	Ö	×	တ	œ	×	д	1	E	Д	Z	œ	Z	œ	œ	Ö	œ
						ī	(	כוס								

Title: Genes Determining Cellular Senescence...

nventors:

Leonard P. Guarente, &

cca gtt ctt tct acg gca aca act ctc tga aca gca att cac aga gct ccc tct tct P V L S T A T T L \* T A I H R A A P S S ctt tag gaa cac agc ctc agc ccc agc ccc agc agc aga ata aca acc tgg I  $\star$  E H S S L S P S P S S S P I T W cat ttg tay ctc ctg ccc cag tca tca tta gtt cct cag ctg cao aag cag ctg  $^{\star}$  L L P Q S S L V P Q L H K Q L cay oft cay caa aty yay cay cty yty yty ofty ofty yaa caa caa aty Q  $\,$  L  $\,$  Q  $\,$  Q  $\,$  M  $\,$  E  $\,$  Q  $\,$  L  $\,$  V  $\,$  L  $\,$  L  $\,$  E  $\,$  Q  $\,$  M cgg tgt tgg oto R C W L ່ 1 1951/651 1831/611 A A 1891/631 1651/551 3 a s ບ 凶 ctg ayd aaa cgg ato ccc ttg tgg cag ~ gtc tgg cag cag L C C 1861/621 1981/661 1801/601 1921/641 <sub>د</sub> « ß

FIG. 18E

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Inventors: Lec

Leonard P. Guarente,

cct P ctg aag cca agt acc gca gtg caa gcg gcg I, K P S T A V O A A taa acc tgg gag gac tca cga atg \* T W E D S R M agg gad cag gad att cad aga 2371/791 2191/731 2311/771 2131/711 tgo ato tco cta gto gat cct ctt caa gtg act ccc tga CCB ctg ctg ctc cag ccc agg gct ctg ccc agg ctg CCA yac ccg tyg gca gea get tga eee gca gtg gct 2281/761 2221/741 2341/781 **4** 0 ø

inventors:

Leonard P. Guarente,

gay god acy too tgt cat tgg cad tad aga tgt atg got god gtg tta tod aga aag otd acg tca ggt cca gat tca ttc agc tga aac tgg agc gtg cca cac cag ctg agc gcc agc ttg tct cca att tac aac tyc ggg aga ttg ctg gac ata taa tgg aat ttt ccc aag acc agc atg cca goo tot toa goo cga goa goa cto ttt tot ott cot otc gtt tgo gat atg gaa tgt ctt tgg cag aac gga att tto gaa aca aco I F E T T tto aga agt tot ttg aat ttg goa gto ttg aac aga age tgg tea atg aaa tee tee agg etg eet aee aae tea tgg tgg atg S 2731/911 2791/931 2671/891 2491/831 oty aty toa tyo ott oty yoa yya yoa yyo Ö 3 ප 2821/941 2701/901 2761/921 2641/881 2581/861

Docket No.: 0050.1491-005
Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarente

2881/961	, 4	4.4	Š	Ş	3			2911/971	/971	<del>(</del>	į	5	. 4	÷	ξ		÷
רנמ י	ניני פיני	ו ניני	Cay acc	) 5 5 5 6 6	ည်း	ងឫង	א א	aya cyy a	י קלקי יי	֚֡֝֝֟֝֝֟֝֟֝֝֟֝֟֝֟֝֟ ֓֞֓֞֓֞֓֞֞֓֓֞֞֞֞֩֞֞֞֓֓֞֞֩֞֞֩֞֩֞֞֩֞֩֞֡	֧֓֟֝֟֝֟֝֝֟֝֟ ֓֓֞֓֓֞֓֞֩֞֩֞֞֞֩֞֞֩֞֞֩֞֞֩֞֞֞֩֞֞֞֞֩֞֞֩֞֞֩֞	ממכ	ָ קַּי	א ביב	) ) 	ת מ מ	נ טני
		<b>,</b> ;	د د	<b>→</b> '	n	ء ۽	۔ ت	٠ ،	_ ;		ָ ק	. E		. 3			<u> </u>
	מ	<b>-</b>	×	24	4	Ħ	E	2	פי	Ω	<u>ی</u>	÷	<b>=</b>	Σ.	74		3
	24	ß	Ω	C	O'	z	E	Σ	>	ĸ	도급	1	٩	U	=		_
								2971,	/991								
•	tga	aag	ato	Ja	atg	gca	ato	acg 1	egg .	tto	aga	aat	gca	5.	aat	gtg	tac
	•	· '×	IR		· ~	<b>A</b>	<b>—</b>		- - -	Ē£4	· œ	z	A			>	×
	H	~	ß	R-7	3	ø	ß	æ	9	ಭ	闰	X	=	_	Σ	ບ	ij
	×	۵	O	Z	Ö	Z		>	>	Ö	×	ບ	H	Ħ	ບ	>	œ
			3001/1001					3031,	/101	_							
	ctt	tgc	aat	tta	tgc aat tta tca tog	tag	atg	cgt 1	tta	agg	gac	agg	tat	Ď,	cat	tat	CCB
	<u>, 1</u>	່ບ	z	ı	S	ಬ	Σ	<b>~</b>	ı	~	<u> </u>	×	×	•	4	<b>&gt;</b>	e.
	ĵz.,	×	H	_	=	R C	ບ	>	*	හ	H	Ö	H	.,	7	H	Ħ
70	7	O	Ē	H	Ħ	Ω	ø	£	×	Ö	ø	>	Œ	K	1	ໝ	₽
		ı						3091	/103	-4		•					
٠,	atg	gct	gca	ag	tga	tta	aga	gaa	tca	tgg	ago	act	gta	8	ctg	acc	aga
•	×	A.	4		*	Ē	<b>~</b>	E	ß	32	S	E	>		7	Ħ	<b>~</b>
	3	J	ဌ	ťΩ	Q	ខា	ഥ	z	а	ರ	K	1	ಭ	٥.	ը *	ы	
÷	Ö	ບ	ĸ	>	Η	ø	×	·H	1	田	=	ပ	1	ш	Ω	œ	Ħ
								3151	/105	-							•
ø	ttt	tag	agg	g	ctc	acc	agc	aca	cag	agc	agc	ttg	ago ttg tac a	39	atc	aat	atg
	F I S H		R S 1	လ	Fe.	T S T	ß		ø	ß	S	J.	<b>×</b>		Н	z	¥
	5±	~	ပ	æ	S	ы	¥	=	×	K	K	ပ	Ħ	רז	Ø	H	3
H	7	ΈÌ	团	1	=	O1	×	Ħ	Ħ	ø	ı,	>	ø	Ω	ø	<b>&gt;</b>	O
	3181/1061							32	/101	_							
b	taa	tca	aac	atg	tac	tgg	ag	acg	gta	gtc	atg	agg	ata	Aa	gca	aaa ttg	ttg
	*	လ	z	<b>5</b> .	<b>&gt;</b>	3	ß	Ę	>	>	ľ	æ	-	¥	4	×	-
	Z	д	H	ບ	Η	G	K	×	ഗ	ß	*	O	*	×	æ	z	ပ
>	H	œ	=	>	ı	对	=		æ	<u>r</u>	Œ	Ω	×	ß	×	H	>
	3241/1081							32	71/1091	<u>_</u>			-	-			
8	tcc	эg	gca	ıtg	cac	ttg	tat	tg	gta	agc	aca	aat	έg	Ċaa	CB	atg	ttg
	ಬ		<	_	<b>.</b>	r	×	*	>	ß	H	z	7	œ		z	7
•	д	یہ	œ	ບ	H	ບ	H	FI	S A Q	K	œ	H	ບ	I C K	Oi	ຍ່	ບ
H	<b>~</b>	G	Z	>	7	>	1	<b>ω</b> .	O <sup>4</sup>	=	¥	ĬΞ	K	ຜ	Z	>	>
								FIG.	18H	Į							

0050.1491-005 Docket No.:

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarente,

ctg gcc ago gga aga tcg tca tyc A S G R S S C tgg aga agt gtg tta ctc acg cct cac gta cgg agc gcg ctg tgc tca tcg atg agg tgt tay ggc cca tct gtg gcc cta gtg tag agt ctg aga cgg 3331/1111 caa atc caa cca gca acc aga aat gtt tet gag gea gtg tea eee got cca ago tgg aga agt act aca tga aga acg ata aga tcc ggc ccc aca tcg caa ctc gee cae tgg

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Separcence...
Inventors: Leonard P. Guarente al.

	gga aaa	×	×			a att	<u></u>	T + O I T & A T A	2	) :	tac ttg tac ata ggt aac caa tgt aca tgg gag	, E	æ	77		g gtt	· >	1	<b>3</b>	;	q ata	'n	K K K E K K E K V F S S	₩ ₩		A AAA	×	×	Q I A L P H L L I L V K N		tga att gta gtt aaa tga, bcc caa act ggc	g	K
			Ħ			ot	-	*	_	•	tg	3	Ö	Ū		ď.	· >	3			ta	*	ß			ta	*	×			ac	H	H
	agt	ß	>	3		taa	*	_	=	•	aca	Ħ	=	Σ		agg	, =	Ö	O		ttt	<b>1</b> 24	Ŀ	1		tag	*	Ø	>		CAA	ď	×
	acg	=	<b>~</b>	되		aat	z	-	<u>, -</u>	3	tqt	່ ບ	>	×		tto	ĵ.	ໝ	0	t	qqt	, 0	>	Ē		ttt	<u>5-</u> ,	<u> </u>	L		paq	<u>d</u>	a
	tcc	S	Д	=		ttt	<u>F</u>	בי	*		CAA	a	Z	Z		act	E	1	<b> </b>		AAA	×	×	×		tca	ໝ	=	Ħ		tga,	*	Ω
	aaa	×	z	H		ttt	<u> 1</u>	E.	<u> </u>	•	AAG	z	E	д		gaa	四	×	Z		qqa	; 0	妇	×		toa	ß	Д	-		ааа	×	z
	atc	H	Ø	O	t	att	<b>,</b>	, E.	<u> </u>	•	ggt	5	>	*		gtg	· · >	3	ບ		aaa	×	×	~		acc	Ŧ	24	1		gtt	>	1
7	aaa gga atc aaa tcc acg	<b>5</b>	ാ	Z	7	act	E	H	>		ata	H	*	~		cat	. <b>=</b>	Œ	ບ	=	aaa	×	×	×	1	CCC	.Д	Д	=	7	gta	>	*
1071/101	aaa	×	×	<b>~</b>	1/1271	tat	່ວ	>	>	/125	tac	<b>&gt;</b>	H	Ħ	/131	tca	ß	=	H	3991/1331	aga	· æ	妇	×	./1351	tto	וצו	ß	а	/137	att	,Η	-
,	aaa	×	×	¥	81	GA	H	=	Σ	3871	ttg	ı	ບ	>	3931	att	H	趾	بعثا	3991	ABB	×	×	×	4051	ctc	П	Ŋ	1	4111	tga	*	Œ
	tca	ಭ	д	O		ata	H	*	Z	;	tad	×	H	h		tat	×	н	X		AAA	×	×	×		tag	*	ß	K		gtt		Œ,
	tcc	ß	а	7		Cad	=	E	=		gga	່ອ	Ω	H		ato	H	ល	1		aaa	×	×	×		aaa	×	z	H		gaa	E	×
	CCC	Ь	ď	Ĺ		tta	П	X	H		ata	I	*	<b>~</b>		tgt	່ນ	>	×		ttt	ъ.	ľ	*		tgc	ບ	K	ø		tga	*	Ŀ
•	act	=	1	മ		tta	ı	* T Y X	H		tgt	ပ	>	X		tgt	ບ	>	H		agc	ູນ	¥	1		ttt	Sr.	Ŀ	1		acc	-	ď
	att	H	1	<b>&gt;</b>		att	<b>)</b>	ĵz,			tgg	3	೮	>		CAC	=	Ħ	Ţ		aaa	×	×	×		aag	×	ß	<b>у</b>		aaa aaa acc tga gaa	×	×
:	agg	 ≃	Ö	Ω		tta	Ţ	*	Z		tac	×	Ħ	J		gtt	>	ĵz.	ß		ลลล	×	×	×		gga	ල ල	4	ø		ява	<b>×</b>	×
1	rco Co	മ	4	œ		god ttt gta aat tta att	z	<b>+</b>	Ŀ		goo oty oty ttt tac tgg tgt ata gga	ĬŽ.	Ŀ	ı		you ada tat ttt gtt dad tyt tyt ato tat att toa cat gtg gaa act tto agg	Ē4	П	ပ		aaa	×	V * Q K K K A L B	×		gaa	Ä	Ы	I. P G R		AAC		E
	5	- \	<b>«</b>	1	1.	gta	>	*		-11	ctg	Ţ	ပ	>	-	tat	<b>&gt;</b>	H	Ce.		aca	ī	ø	×	-	ctg	1.	3	Ü	_	_		×
4	g g	9	>	-	//126	tt	<u>-</u>	1	ပ	3841/1281	ctg	Ţ	ပ	4	/130	aca	E	=	H	/132	tta	ľ	*	z	/134	tgc	ບ	<	Д	/136	aac	z	₽
4.4.	a G	ر در	>	3	3781/12	dcc	æ	а	J	3841	gca	æ	4	വ	3901	gca	4	a	æ	3961	ggt	<del>د</del> ع	>	ß.	1021	att	_	노	-	4081	aca	_	ď

tat ata tat ata tat aat gaa aaa ggt tto

att taa cac tgt tta taa aaa ata tat ata

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarente

yta ttt tot tgt ttt gat gto taa tot gta tot ata atg tac oot agt 'agt oga aca tac cgt att ttg agg atg gga ggg tgt gat tgt tta atg act act gga ttt ttt tat att att gaa agg taa aat ctg att att tag cat gag aaa aaa aat cca act ctg ctt ttg att aag ttt atg aaa tto taa aaa atg cot ata tat agt gta tac ttg gtg tag act ttg cat ata tac aaa ctg ttc gtg agg agg aga tgc gag L F V R R R C E 1531/15114291/1431 aaa gct tca gtt tgt ttg ott ota aga gtt gct ttg gag act 4501/1501 4381/1461 4441/1401 4321/1441

Title: Genes Determining Cellular Senescence...

nventors:

Leonard P. Guarente, e

ttt tya tit tgt gac agt caa aag gac gtg caa aag tct agc ctt gcc cga gct ttc ctt F \* F C D S Q K D V Q K S S L A R A F L tct aaa tgt tat tca aga ttg agt tct cac tag tgt ttt ttt aat cct aaa aaa gta atg tca acc aga agt aaa ttt ttt tgt ttt gaa gga ata aat gtt ctt tat aca gcc tag tta atg ttt aaa aag aaa aaa ata gct tgg ttt tat ttg tca tct agt ctc aag tat agc gag att ott ttt ggt aag aaa aga gaa tta goo ago oot gtg oat toa ttt tya ttg tac aat tgt aca ttt gta tac ctg taa tgt aaa tgt gga gaa gtt taa att att ctc acc ttt tat ggt cgt agc ata tag tgt tgt ata ttg 4831/1611 4951/1651 aac ata aac acg ttt 4741/1581 4861/1621 4921/1641

FIG. 18L

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarent

atg ctt atg cct ggg caa cta ttt tt gta act ctt gtg tag att gtc tct aaa caa tgt N L M P G Q L F F V T L V \* I V S K Q C act cca atg aac ttt ttt gca ago aca ctt gta acc ata tgt gta taa tta aca aac otg tgt aca atc aga gcc cct ctc acc ttg taa agt gtg aat cgc cct tcc ctt ttg tac aga aga igt tig aat ata gaa tig taa cac tac acg gig tac att icc aga goo tig igt taa cat act 5011/1671 5071/1691 5191/1731 5251/1751 gtg atc ttt att ttg aaa aat aca gaa ctt v I F I L K N T E L att ttg tct act tgt 4981/1661 5161/1721 5221/1741

FIG. 18M

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarente

GAA CIT TGA GAA AAG TAT CAC'AAA ACT TGG TAN GCA GCA NGG GGA CAA ATC ACC AAA GAA CAA O K CI GAA AAA GGG IGT AAA GCA GTT CAA GAA TGG ACC TAA AGT CAC ATC AYY CCA GCC GGC AAA TI P A G K \*
F Q P A N S S R Q I TAA AGA AGG T \* R R F K E G K K V

FIG. 19

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarent

al.

TIGT TCG GGC AAA GCA GAT C S G K A D V R A K Q M CTT CAA AAA GAA GAA GAA AGA ACT GAA TGC ATT TGC ACA CGA TTC AAC C I C T R F N A F A H D S T TGA CAA AGA AAA AAG AGT AAA GTT AAT \* Q R K K S K V N D K E K R V K L M TAA AAC : TYP GCA GAA GTT GAT TCA AGG GAA AAT

P A E V D S R E N

L Q K L I I Q G K I AGC AGC CAA GAA GCC CAA ATG CAG ACA ACT CAG TGA TAA AAC Ci 3. ATC AC I S E S N Q 361/121

Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarent al.

TGC AGA GAT ANT CAG AAG TTT TAA AGG CCA C R D N Q K F \* R P TICA ACA ACA GAG AAA ACA GGC TTIT TICA AGA AGC CAA NTA TIC GAG AAA TAT TGT TAA GAA GAT ACA T GIG I'T'A CAT' I'CA GI'A I'GG ATT GCG AGA TIGA TITT GGT TIGA GITT AAG ATT TOT CAT GUA TGG AAG TAA ACC I S II V W K \* T 661/221

FIG. 19C

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence... al.

Leonard P. Guaren Inventors:

ÇCC GAT TYCT AAC TYC AAT GGC CCA AAA GGA AGC D. S N S N G P K G S CCG CGN NGC GGT GGT CTN CCT GGC NCN CAC CAA AGO CAT TITT GGA GCA GAG GAA CAT GCT GAC GGA AGA GCT CTA TGG GAA CAC AFT TCA GGA CAN NST GIT AGA GGT ACA GCC AGA AAA AIT CIT GGA CIT ITT TAC CIA TGC ACC 961/321 TGT GAT TAA GCA CTC ATT GGT GCA TAA AGT C D \* A L I G A \* S ATT AGA ACT TAT TAT GGA TGA AAT GAA ACA I R T Y Y G \* N E T L I N D E N K Q CAA ACT CAG ATC AGA AAT GAT TGA AGC CAT AGC AGA TYCA CCG AAC TYCT  $C_i$ SIC Cı GCT TTA CAA 1021/341 108/106

ngspasses ounsite

ACA CGA TYG CGC CAG AGT GGC CAT GCA CTG

Title: Genes Determining Cellular Senescence...

Leonard P. Guarente,

CAT AGT AAA TGA CAA ATA TGG AAG H S K \* Q I W K

nventors: TGA TGA TAC TAA GCT TGT GAA GCA GAT AAT COT GIG OCA ING CAC GCC CAA GGA CAG GAA

TEA AAA GET GEC TAA TEG CCA ATA CTC ACT GAT TGT GAA AAC AAT GAA GAC 1141/301

TTG TAT TYT GGT TYT ACT GGC GGC ATY TGA 1201/401

ATT GCC TAG CAG TYTC CAT ATC AGA AAT TAT 1261/42

CCT ATT GTA CTT ACT AAG CCC CAG AGA TCC TGC ACA TAC: AGT ACG AGA AAT CAT TGA AGT

0050.1491-005

hventors:

Title: Genes Determining Cellular Senescence... Leonard P. Guarente, e

TOT GON NAN NGG NGA TGG AAA TGC ACA CAG TAA GAA NGA TAC AGA GGT CCG CAG ACG GGA 1411/471 1381/461

GIC IGA CAT I'CT GGG AI'C I'GC CAC I'GG AGA CCA AGA AGI GTT ANG CTA CCT. GCA AGA ACA. CGC GGT GGT GCT AGA TAA GTC TGC GTG TGT GTT GCT CCT AGA ATC CAT TTC TCC AGC 1501/501

CITY GGC AGC AAC AGG ACT GCA IVC TGG CAG CCT TOA GCC THE CAT GAA TGC CAT CGC

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarente

THE THE THE THE CET CET CEA GAG THE TGA CET GGA MET TGE AAA CAA AGT CAA AGE TGE ACT GAA AAG CTT GAT TCC TAC ACT GGA AAA AAC CAA AAG CAC CAG CAA AGG AAT AGA 'AAT T E K I, D S Y T G K N O K H O O R N R N TIGG GAG MGA AGG TITG ITT! TIGG AAA AAC ACT THE THE MEG MEN THE THE GAN GIVE GIT TGC NOT AGA GOA MOT TWO TAT GAA GAA CCT GAA GTO CTG GGO TAG TGT AAA TOG AGG 1891/631 AAT AGA GCA NGA TAA AAA GAT GAA AGA AAA CAA GGA CGG NGA GCT TCA CAT TGC AGA ACA r S 1001/601

Title: Genes Determining Cellular Senescence...

Inventors:

Leonard P. Guarente,

AIT! GGG GIA CIC 11CT ATA 11CT GTT 'TCT TTG TAT! ACG AAT CTA TYT ATA TAA ATT ATA GGT GGA AAG AGT TAA GAG CAA GAT GGA ATG ATT 1951/651 TOT GIT CIC INT TOT GIT TOC CAA INC I'CT ACT TGA AAA ACT GAG CAC 2041/681 1981/661

FIG. 191

2101/701

0050.1491-005

Title: Genes Determining Cellular Senescence...

Leonard P. Guarente,

1079 1456 1154 100**4** 120 779 45 845 70 929 95 346 5 435 4 704 20 624 172 8 262 9 524 15 TT'I'TCG'ICTCATTACTGATATCCAACTAACAGTCTCC'ICATAGACGGTACCTTACTTTTCC'ITTAATATTAAAATACTAGTATAGTCGCACATACTTAAC CCT P AGC S AAC N TCC S AAG K CAA TGA TATATAATCGATCGCTCTCGTAGTTGATATCCTCTCTCTTTGCTTTTTCCTGTATATAGTAT ATG TGT ACA TAC AAA K T'TA TAC gcc A AAA K GAG TCG GAC TAC TTG TAC CGT ACC AAC ACT GAT ACC Y L Y R T N T D T ACT T GAA E AAC TAA GCGCCGATT ATG GGT GGC N \* M G G TCT S ACT GTA GAA TCT GCT GCT ACT ACC ACT ACA TTG TCC TCA TCT T V E S A A T T T T T L S S S ACT T TCT S GCG ATA CTC CGA TTT' F AAC CCT P CCT P TCT GTC GCA S V A T'IC TGG W GTC V GAC ATG GAT GCC D M D A CAT TAG ACAATAACAGCGACAATTAACCTAAAGAGGATAGAAGATCGAGCAAAAAAATTTTTAAT ATG GGG TCA GTG TCG GAC S AAG ACT CAA K T Q CGC R GCG A TCT S TTT TGA CGGCAAATAG ATG TGT CCA P CTT L GTC ATG ( AAA K AAAK TCA TCC S GGA\_ATG GTC V GAA E CGA R TCGTCTCTCTAACACATA ATG AAA ATT TCC GCA GCT TTA ATA TTG TCT M K I S A A L I L S CAT CAC AAA GAT II H K D ACT T TCT S GAT GGT AAA TCT GTT GGT GGT CTT TAT TGT AAA AAT GGT D G K S V G G L Y C K N G GAA CTC (E CAA GAT GGT Q D G GGA TGG GCC G W A TGT GAA CCT C E P ATT I GAG AGG ATC E R I 'FAA AGAGTAAGTTGAGTGTAAGGTGGTAGAATT ATG TAT GCA ' GAT D T'TC F GGTTTT GGA G GAA E TAT Y CAT CAT TTG . TAC ATA GAT TCC AAT GCC GCT ACT AGT
Y I D S N A A T S TCT CAG AAG CGT GAT GGC Q K R D G TTG GAC TGG CTA GGA L D W L G TGG W GIT AGT V GGC TAC TAC TGT G Y Y C ATA I GAC AGT D S GAA TAT ACC TCA E Y T S TAC Y GCG A GAG GCA ATT E A I GAT D CCA P AAG K GCT T'AC Y NGC S AGT S NGC S A'TA CCT P ACC T TGT A'TG M GAC AGA R CCA GCA GAA GAT D GGT G 263 347 6 436 5 173 525 1080 146 96. 625 705 780 46 855 71 930 96 1005

FIG. 2

1229 195

CAA CCA

GAT TCA (D S (

GGT GGA G

GAT D

GTT V

GTG V

TCT GAA AAC ATG GTG ATT CCC ACA S E N M V I P T

GAT

1.230 196

TCC ATT

AAG TCT GAC K S D

AAA K

GCT AAG GCC ATT AAC A K A I N

TCT

ACA T

TCT ACG GAT GAA S T D E

1155

1379 245	1454 270	1529 295	1604 320	1685 1	1760 26	1838 5	1913 30	1998 5	2072 23	2160 3	2245 15	2331 10	. 2406 35	2457 10
1305 GAT GAA GAC ACT TAT TAT CAA TGG CAG GGT AAA AAG ACT TCT GCT CAG TAC TAT ATT AAC AAC GCC GGT GTA TCT 221 D E D T Y Y Q W Q G K K T S A Q Y Y I N N A G V S	1380 GCA GAA GAY GGG TGC ATT TGG GGT ACT TCF GGT TCG GAT GTC GGC AAC TGG GCT CCA CTA GTG TTA GGT GCT GGT 246 A E D G C I W G T S G S D V G N W A P L V L G A G	1455 TCC ACT AAT GGA GAA ACA TAC TTG TTG ATT CCA AAC CCC AAC AGT AAC CAA GCT GCC AAC TTT AAC GTT AAA 271 S T N G E T Y L S L I P N P N S N Q A A N F N V K	1530' ATA GTT GCA TCC GAT GGC GCT AAC GTT CAG GGC AGC TGT GCG TAT GAA GAT GGC TCT TTC ACC GGA GAT GGT TCC 296 1 V A S D G A N V Q G S C A Y E D G S F T G D G S	1605 GAT GGT TGC ACA GTT TCT GTT TCT GGA TCT GCT GAA TTT GTT TTC TAT TAA GTCACTCTTTTTCGGTAAAAGA ATG 321 D G C T V S V L S G S A B F V F Y *	1686 TCT TGT ATT TTG ATA CCC TCA ATT CCC CTT ATT CTT TTT CTT C	1761 TTC CGT TAT ATT TTT CTC CTT TCA GTT CAT TTT ACT TCT TAA AAAGTTTCGTTGATCGCTATT ATG CTA TGG ATT CAA 27 F R Y I F L L S V H F T S *	1839 AGA TITI TCT TCT CTT CAA GGT GTA CTC TGC ATT ACG GTT TTC TTT AGT TCG TTT ATT TTT TTG TTA 6 R F S F L S L Q G V L C I T V F F S S F I F L L	1914 ACA AGG TGT 1TG TAT ACA TAT ATA ATAT ATG GAA ATA TTA TAG TGTTTATTTTTGTTACTTCCTGCGAGTTGCAACAGAACTA 31 T R C L Y T Y I * M E I L *	1999 ACAAG ATG CCA TGC TGT TTT TTT TTT GGC TAT AAA AAT AAC AGT ATC CTA GTC CTT GTG TTC GGC TTT 1 M P C C F F S F G Y K N N S I L V L V F G T	2073 AAA ATG GAA TTG CAA ACC CCA TAA TTCCTTCTTCACAACGAACAACGCCTAGTAGTCGATTTTCAGAGACTCTA ATG CTT TGA ATA 24 K M E L Q T P *	2161 TAATTTTTTTCTTCAAAATTTCCTTAAGCGTGCTATCGA ATG AGT AGA CAT CAA TCA AGA GIT TCA TGG TCT CCC CGT ATT TGC 1 S R V S W S P R I C	2246 CGC TGC TTC TAA TATTTTTGGAGTGTAGCATAGCCCAATCAATCAATCTTCGATA ATG CCA CTT TTT ACA TAT ACA CGA CGA CAA 16 R C F *	2332 CCC ACA GTA GTA ACA CTC ATG ACT AAA TTT TCA TCA GTA CTT AAT GTC ATG TAA GGG GCT AAC GAA ATC AAT GCA 11 p T V V T L M T K F S S V L N V M L G A N E I N A	2407 ANG GGC GIT TOT CTA TAA ACG ATG ATA TGC GTA TTG TTC ACC ACT GGA TCC
-	-		- ·	_	П	_	)	7	-	7	2	7	73	CA

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...

Inventors: Leonard P. Guaren al.

1039 1189 1114 184 1264 234 109 589 9 739 59 814 964 256<sup>4</sup> 406 501 664 34 331 69 1GTT11AGTGCTACCCAACTACTTACATTCCT1TTAAAAACCACAAATATTTAAGTTAACCTGAGCTTTATTTTTTTAGTAAGTTATTTACCACAATTTTTCTCA GCA TAG CACAGCATAGCAGCTGTGTATATCTTAAATAAG ATG TAG ACTGGTTTGGCATTTGGAAAGGTTTTGTGTAAGAAAAGCAATAC1"TGAGGT A \* AGT S AGC S AAG K ACT T GCT A GCT TCT S TTT F ACG T TTT CCA ATA CCG F P I P CAT H TCTTTTGAT GGC CAC ACT GTA ACT CCT GCT D G H T V T P A GCA TTA GGA AGA ACC AGA AAA TAG CCATTA ATG CTT L G R T R K \* CAC CAA O GCT CAA O GAA ၁၁၅ TCC ACC ၁၁၁ TCC GGA CAT S G H GAT ACC GCA TCC CCA ACC TCC
P T S CAA CCC GAA GAT E D TCC TCT TCTCGT ACT CTT TCA ACT TCT CGA GAG AAA ATC E K I ACT GTT V TTG GCT L A TAT TCC GCA ACT AAA K GTT CAC CAA V II Q GCA GCA TTT $\operatorname{TTT}$ TGG TAC GAA ACT GTT GTT GTC GAT TCT Y E T V V V D S GTG AAT GTC GTG ACT T ggc TCC S ACT TCT S AAG GAC D GAT D TCC S TCT TTT F TCT S TGC TCA GCT C S A GAT GCG CAC GTG ACT CCA P ATT ACA ACA I T T TCCTTA GCC CTC AAC CGC TAT ACA TCC CCA ACA TCT
P T S ၁၁၅ TTA CCA L P TCT S TTT CCT AAG GCT K A TTC AGA 7 GCT GTG V AAA GCT A ACC T GCT GGA AGT S TCT S ACT T TCTAAT N GAA TTA L AGA R GTT GCG TAC AAA TAC GTT V A Y K Y V gggAGT S ANA K ე<u>ე</u>ე GTG V ACC TACACCTTTACAATCCGTATTGCC ATG GAA TGC C AAT N GAG E ATC I CAA AGT S GCTGCT GTC V TCT AGT AAT N GCC A GCT TCT S AAA AGT. GTT V A'l'T GCG TCA AAC N GNA E ACT TCC ACA T GGT G TCA CAA Q TCA CAC TCT. S GCT A GCT TTC CCT P CGT AGT S CCC GCC A A'I'F ၁၁၅ CGTGAA E CGT R 1'GG AGG TCA S 999 GAC 740 890 110 182 257 45 665 35 815 85 965 135  $040 \\ 160$ 115 210 502 1 590 10 332 407 101

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Senescence...
Inventors: Leonard P. Guarente,

			_								
1339	1414 284	1489	1564 334	1639 359	1714 384	1789	1864 434	1939 459	2022 476	2108 14	2150
TGC	TCT S	TTA L	TAC Y	CAA	GAA	ACT	GTT V	999 9	GCTACGTGACTACTTTTTCCTTTTTTTTTT	CCT	
TCA	CCA P	TAC Y	GAC D	GAC	GTT V	TCC S		gac D	TTTT	CCA	
GGT G	CAA	GAT D	ACC T	GTT V	TCA S	200 3	AAG K	GCT	יככזיו	TGT	
၁၅၅	GAT D	GCG A	AGA R	GTT V	GTC V	GCT A	GTC V	GGT G	TTT	TAC Y	
ACT T		GAC D	TGC	ACC T	၁၅၅		AAC	၁၅၅	CTAC	. TTA L	
TCC S	CCA P	ACT T	ATT I		gcc A		TAC	TCT S	ACTA	TAT Y	
ACT.					AAC				CGT'G.	CGA	
GAC						TTA		GAG	3CTA	TAC	
ACC (T		CGT 7						GGT (		'ryr F	
AAC N	AAG K		AAG (			GCA (			AAT '	TCT S	
GAA 1						TGG (			TAC 1	TTT F	
GTG (	ATG 3					AAC 7 N			TTA 1	CCC P	ບ
GGT G	GGT	GGT '	AAA (	GAA (E	GCT (				GTC 7	GTC V	TAT Y
TCC	CCA	AAT	TCT	GTT	TCT	ATT ( I	CCA	TGT	TTC	ATG M	CAT H
TGG W	CAA	AAA K	GTT V	TAT	ACA	GGT G	AAC	GAA	CAT	CTCACACAATCACT	T'AC Y
GGA G	TGC C	TGT C	GTT V		AAG K	TCT	CCT	GGT' G	GCT	CAAT	CTG L
GGT G	TCC S	$\frac{\Gamma}{L}$	TAT Y	CCA P	AAA K	GGA G	ATT I	ATC I	AAA K	CACA	TTT F
GAG	TAC Y	TTG L	GCC	ATC I	၁၅၁	TCT	TTG L	GTC V	GGT G	ACCT	TCT TTT CGT TAA TGGCCTCA ATG S F R * M
၁၅၁	TCC S	GGT G	GCT A		GAA	ACT T		AAT N	TCC	CTAT	CTCA
	TGT C.	0 0	GAG E	ATG M	TGG W		TTA L	TCC	ACT T	ວວວວ	TGGC
TGG W	TAC Y	GTC V	GTC V	AAC		TGG W	TAC Y	TCA S	GTT V	CTTTTTTTCGAACACATCTCACCCCCTATAC	TAA *
GAC D	TCC S	TCT S	GGT G		TTT F	ATC I		GAT D	TCT S	ACAT	CGT R
ATT I	000 0		T'GG W	ACT T			GTG V	GAT D	GTC V	GAAC	'l''l'' F
TCT S	GAG	GGT. G	GAA E	00C 0	AC'I'	000 0	GGA G	GCT' A	ACC T	TTTC	TCT S
ATT J		GAC D		CCG P	GAT D	GAT	GGT	GCT	7.GT C	CTYFT	T"["]
1265 235	1340 260	1415 285	1490 310	1565 335	1640 360	1715 385	1790 410	1865 435	1940 460	2023 1	2109 15

100 ALILSSLSSV LLALS AVT.TLISSG	150 AVVIPAA HTVTPAASEV	200  AAATTSAAAS KISDAAASAT	250
SRNSSMKLSA SRNSSMKLSAMKFST	TVTQYID TVTQYVNADG YETVVVDSDG	ATTTL AATTTLSSTA VSSAALAKNE	EAAPTSTVVS
LNKNLPSLNF	EKPAVV DKRAVV .KRAVAYKYV -K-AVV	AATSTVES.A AADGKVESVA AAADSSASIA AAS-A	ODGTVKC EDGTISC ESSSVSSSSE
FEYNQLLVLP	DSHHEDIIHKD VHHSDNHHN VHQEDAHQH.	'I'TATSA TSVLAPTSSA	TSEQKRDGGF SSSSVGSGDF SSSSSATSTL
VYFLFIHSFL	101 AFSAPAPAPA ASTAVLAAPA AIVSALPHVD	151  ATAATSAIIT	201 SSSEKD SSSSSSSSS ASTEQGASSS
Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus	Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus	Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus	Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus
	(Nca3)MKISA ALILSSL. (Uthl) VYFLFIHSFL FEYNQLLVLP LNKNLPSLNF SRNSSMKLSA LLALS. (Sagl)MKFST AVT.TLI.	(Nca3) (Uth1) VYFLFIHSFL FEYNQLLVLP LNKNLPSLNF SRNSSMKLSA LLALS. (Sag1)  101  Nca3) AFSAPAPAPA DSHHEDHHKD EKPAVV TVTQYID  Uth1) ASTRAVLAAPA VHHSDNHHHN DKRAVV TVTQYVNADG AVVIPAA Sag1) AIVSALPHVD VHQEDAHQHKRAVAYKYV YETVVVDSDG HTVTPAA.	(Nca3)      MKISA ALILSSL.         (Uth1)       VYFLFIHSFL FEYNQLLVLP LNKNLPSLNF SRNSSMKLSA LLALS.         sus      MKFST AVT.TLI.         101      MK-SMK-S         (Uth1)       AFSAPAPAPA DSHHEDHHKD EKPAVV TVTQYID         (Uth1)       ASTAVLAAPA VHHSDNHHHN DKRAVV TVTQYVNADG AVVIPAR         (Sag1)       AIVSALPHVD VHQEDAHQHKRAVAYKYV YETVVVDSDG HTVTPAR         Sus       A

Title: Genes Determining Cellular Serescence...
Inventors: Leonard P. Guarente al.

300SDFPSV NGIVSLDWLG FGGWASVMDM DANTSSECKDSDFPSG QGAVSLDWLG LGGWASIMDM NGNTATSCQD SATKSSTSST SPSTSTST SSTSSSSSS SSSSSSSNT DTSTGGSCKE	GYYCSYACEP GMSKTQWPSD QPSDGKSVGG LYCKNGYLYR TNTDTSDLCS GYYCSYACSP GYAKTQWPSE QPSDGRSVGG LYCKNGKLYR SNTDTNSLCV GSYCSYSCQP GMSKTQWPSD QPSDGRSVGG LLCKNGYLYR SNTDADYCLE G-YCSY-C-P GKTQWPS- QPSDG-SVGG L-CKNG-LYR -NTDLC-	TDETSAKAIN KKSDSIALCR TDYPGSENMV IPTVVDGGDS QPISVVDEDT EGOGSAOAVN KVSGSIAICG TDYPGSENMV VPTVVGAGSS QPINVIKEDS WGVEAAYVVS KLSKGVAICR TDYPGTENMV IPTYVEGGSS I.PLITVVDODT A K-SA-C- TDYPG-ENMV -PT-VG-S -PVD-	YYQWQGKKTS AQYYINNAGV SAEDGCIWGT SGSDVGNWAP LVLGAGSTNG YYQWQGKKTS AQYYVNNAGV SVEDGCIWGT EGSGVGNWAP VVLGAGYTDG YFTWEGKKTS AQYYVNNPGV SVEDGCIWGT SGSGIGNWAP LNFGAASTGG YW-GKKTS AQYY-NN-GV S-EDGCIWGT -GSGNWAPGAT-G
FGGWASVMDM I.GGWASIMDM SSSSSSSSSNT	LYCKNGYLYR LYCKNGKLYR LLCKNGYLYR L-CKNG-LYR	IPTVVDGGDS VPTVVGAGSS IPTYVEGGSS -PT-VG-S	SGSDVGNWAP EGSGVGNWAP SGSGTGNWAP -GSGNWAP
NGIVSLDWLG QGAVSLDWLG SSTSSSSSSS	GYYCSYACEP GMSKTQWPSD QPSDGKSVGG LYCKNGYLYR TNTDTSDLCS GYYCSYACSP GYAKTQWPSE QPSDGRSVGG LYCKNGKLYR SNTDTNSLCV GSYCSYSCQP GMSKTQWPSD QPSDGRSVGG LLCKNGYLYR SNTDADYCLE G-YCSY-C-P GKTQWPS- QPSDG-SVGG L-CKNG-LYR -NTDLC-	TDETSAKAIN KKSDSIALCR TDYPGSENMU IPTVVDGGDS QPISVVDEDT EGOGSAOAVN KVSGSIAICG TDYPGSENMU VPTVVGAGSS QPINVIKEDS WGVEAAYVVS KLSKGVAICR TDYPGTENMU IPTYVEGGSS I.PLTVVDODTA K-SA-C- TDYPG-ENMU -PT-VG-S -PVD-401	SAEDGCIWGT SVEDGCIWGT SVEDGCIWGT S-EDGCIWGT
SPSTSTSTST	GMSKTQWPSD GYAKTQWPSE GMSKTQWPSD GKTQWPS-	KKSDSIALCR KVSGSIAICG KLSKGVAICR K-SA-C-	AQYY INNAGV AQYYVNNAGV AQYYVNNPGV AQYY-NN-GV
SATKSSTSST 	GYYCSYACEP GYYCSYACSP GSYCSYSCQP G-YCSY-C-P	351 TDETSAKAIN EGOGSAOAVN WGVEAAYVVS	YYQWQGKKTS YYQWQGKKTS YFTWEGKKTS YW-GKKTS
Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus	Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus	Pile.l (Nca3) Pile.l (Uthl) Pile.l (Sag1) Consensus	Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus

Docket No.: 0050.1491-005
Title: Genes Determining Cellular Ser
Inventors: Leonard P. Guarente,

nce...

451 ETYLSLIPNP NSNQAANFNV KIVASDG.AN VQGSCAYEDG SFTGDGSDGC ITYLSTIPNP NNKEAPNFNI KIVATDG.ST VNGACSYENG VYSGSGSDGC VTYLSLIPNP NNSDALNYNV KIVAADDSSN VIGECVYENG EFSG.GADGC -TYLS-IPNP NA-N-N- KIVA-D V-G-C-YE-GG-G-DGC -TYLS-IPNP NNGNALNFNV KIVAADDSST VNGECIYENG SFSSGGSDGC	
KIVASDG.AN V KIVATDG.ST V KIVAADDSSN V KIVA-D V	
451 ETYLSLIPNP NSNQAANFNV ITYLSIIPNP NNKEAPNFNI VTYLSLIPNP NNSDALNYNV -1YLS-IPNP NA-N-N-	515 FVFYZ FVFYZ FVLYN FV-Y- FVLY.
451 ETYLSLIPNP ITYLSTIPNP VTYLSLIPNP -TYLS-IPNP	501 515 TVSVLSGSAE FVFYZ TVSVTSGSAN FVFYZ TVSVTSGKAH FVLYN TVSV-SG-A- FV-Y- TVSVTAGKAK FVLY.
Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1). Consensus Sun4	Pile.1 (Nca3) Pile.1 (Uth1) Pile.1 (Sag1) Consensus Sun4

Docket No.: 0050.1491-005

Title: Genes Determining Cellular Se

Leonard P. Guarente,

## EIGHT REPEATS IN UTH4

193	LatDqFGcrFLQKkLE
231	LilDpFGnyLVdKicD
267	IsinqYGtrsLQKiID
310	LinDInGnhVIQKcIf
348	IstHkhGccVLQKiLs
384	LinDqFGnyIIQfiLD
422	LsclkFssnVVeKfIK
487	LirDnFGnyALQtlLD

HYDROPHOBIC CHARGED

FIG. 23

DOCKET NO.: 0850.1491-005

Title: Genes Determining Cellular Senescence...

Leonard P. Guarente, Inventors:

UTH4 YGLO23 PUMILIO HUMAN	LatDqFGCRFLQKkLE LckDqHGCRFLQKqLD FsqDqHGSRFIQQkLE FsqDqHGSRFIQLkLE	I
	LilDpFGNYLIQKiCD Lm†DsFGNYLIQK1LE Lm†DvFGNYVIQKfFE LmrDvFGNYVIQKfFE	2
	IsiNqYGTRSLQKiID IslNpHGTRALQKlIE LalQmYGLRVIQKaLE LalQmYGLRVIQKaLE	3 -
	LinDlNGNHVIQKcIF LskDlNGNHVIQKcLQ CvkDqNGNHVVQKcIE CvkDqNGNHVVQKcIE	4
	IstHkHGCCVLQK!LS IatHrHGCCVLQRcLD LstHpYGCRVIQRiLE LstHpYGCRVIQRiLE	5
	LinDqFGNYIIQFlLD LtlDpFGNYVVQYiIT LiqDqYGNYVIQHvLE LvqDqYGNYVIQHvLE	6
•	LscikFSSNVVEKfiK LsiHkFGSNVIEKiiK LsqHkFASNVVEKcVT VlsQhFASNVVEKcVT	7
	Lir Dn F GNYALQT ILD Lln Dsy GNYVLQTaLD Mmk Dqy ANYVVQ Km ID Mmk Dqy ANYVVQ Km ID	8

FIG. 24